REMARKS

Office action summary. The Examiner has rejected claims 1-3, 5-8, 10, 11, 27-36, and 39 as anticipated by U.S. Patent No. 4,552,751 ("the '751" or "Inaba"). The Examiner has also rejected claims 1-41 as obvious over U.S. Patent No. 5,800,832 ("the '832") in view of the '751, and has rejected claims 42-53 as obvious over the '832 in view of the '751 and U.S. Patent No. 5,891,453 ("the '453").

Applicants very much appreciate the withdrawal of the prior rejections.

The pending rejections are traversed.

Preliminary observation. The Examiner writes in the office action:

> Claim 1 is directed to composition comprising
> (1) composition comprising: (a) water swellable polymer, (b) hydrophilic polymer, and (c) oligomer; and
> (2) erodible backing.

(Action at 3.) This is not at all correct: there are other limitations in claim 1 besides those listed by the Examiner, as is easily seen by looking at that claim. For both obviousness and anticipation all claim limitations must be considered. The Office is not legally permitted to ignore claim limitations in deciding anticipation and obviousness. *See, e.g., Kahn v. General Motors Corp.*, 135 F.3d 1472, 1480-81 (Fed. Cir. 1998) ("In determining obviousness, the invention must be considered as a whole and the claims must be considered in their entirety."); *RCA Corp. v. Applied Digital Data Sys., Inc.*, 730 F.2d 1440, 1444 (Fed. Cir. 1984) (stating that anticipation is established only when a single prior art reference discloses, expressly or under principles of inherency, *each and every element* of a claimed invention).

The Examiner also writes "The specific cellulose esters claimed by claims 3 and 11 and the materials of the backing claimed by claims 12-14 do not impart patentability to the claims, absent evidence to the contrary." (Action at 5.) Again, this is legal error. The Office is required to show that the claims are unpatentable, or else allow them. See 35 USC 102 ("A person shall be *entitled* to a patent unless" certain conditions are met); *In re Glaug*, 283 F.3d 1335, 1338 (Fed. Cir. 2002) (Office "bears the initial burden of presenting a prima facie case of unpatentability"). The applicants are not required to provide evidence of patentability of the claims until the Examiner has made out a proper prima facie case, which is not the case here.

Anticipation rejection over the '751 patent. The Examiner's anticipation rejection of claim 1 is in error for at least the following reason.

The '751 patent discloses two different kinds of layers. See, e.g., '751 claim 1. According to the claim, the "drug storing layer" comprises (a) one of HPC, PVP, and HPMC plus (b) a plasticizer, and (c) the drug. The "drug controlling layer" comprises these things plus cellulose acetate or a vinyl acetate resin.

As the Examiner correctly points out, the recitation of elements (a)(i), (ii), (iii) for the hydrogel in the instant claim 1 overlaps with the elements of '751's disclosed "drug controlling layer." This is because that layer (1) contains a cellulose acetate or vinyl acetate resin which might be water-insoluble and water-swellable and (2) contains PVP, HPC, or HPMC, which are hydrophilic polymers to which certain of the '751's plasticizers might hydrogen bond.

However, the recitation of elements (a)(i), (ii), (iii) in instant claim 1 does ***not*** read on the '751's "drug storing layer." In the "drug storage layer," there is no water-insoluble, water-swellable polymer as required in element (a)(ii) of present claim 1.

Thus, in attempting to read claim 1 of the present application on the disclosure of the '751 patent, the hydrogel can only be read (if at all) on the '751's "drug controlling layer." That leaves the "drug storing layer" as the only possible candidate for the backing layer also required by claim 1. See, e.g., '751 FIG. 1 (disclosing only devices composed of a drug storage layer and a drug controlling layer).

However, the "drug storing layer" of the '751 is fairly certain to erode more rapidly than the "drug controlling layer." Adding water-insoluble cellulose acetate or a vinyl acetate resin – as the '751 does to get from the "drug storing layer" to the "drug controlling layer" – tends to slow, not accelerate, erosion in a moist environment. Thus, the proposed read of present claim 1 on the disclosure of the '751 fails. To the extent the "drug storing layer" in the '751 can be seen as a backing layer at all, it does not meet the limitation of eroding more slowly than the hydrogel recited in claim 1. There is consequently no anticipation.

Obviousness rejections over the '832 in view of the '751. The Examiner finds that claims 1-41 are obvious over the '832 in view of the '751. This combination fails to establish a prima facie case of obviousness for at least the following reasons.

A prima facie case of obviousness requires, inter alia, that "there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings." MPEP §2142.

First, claim 1 recites a hydrogel. The '832 expends close to half a column of text to explain why gels are a bad idea. We read there:

> Bioadhesive carriers are known in the art and include gels, pastes, tablets, and is [sic] films. These products, however, *may lack one or several of the preferred characteristics* for an efficient and commercially acceptable pharmaceutical delivery device. . . .
>
> Bioadhesive gels which are used for application to mucosal tissues and especially the oral cavity are known in the art. . . . However, this type of pharmaceutical carrier has a *very limited residence time*, given that body fluids such as saliva quickly wash it away from the treatment site.
>
> Unlike bioadhesive gels and pastes known in the art, which have a *very limited residence time*, given the tendency of bodily fluids such as saliva to wash away the gel from the treatment site, the present invention offers an increased residence time because of its filmy consistency and components. A typical residence time for an aqueous gel or paste, such as Orajel®, Orabase®, or Kanka® is a few minutes. *This short residence time is a consequence of a limited or poor adhesion.* In a typical aqueous gel, the mucoadhesive components are either in solution, suspension, or swollen. Once applied to the mucosal surface, however, the water based gel does not instantaneously penetrate the lipophilic mucosal surface. The composition and water affinity of these gels results in a tendency to quickly mix with the saliva, rapidly pulling away the different components of the gel, and limiting the residence time. . . . The present invention, by its solid form and its instantaneous adhesion to the mucosal surface, allows a lasting contact . . . . Dissolution kinetics in the saliva and other aqueous media are influenced by the physical state of the device. While a gel or solution will readily mix with saliva and/or other bodily fluids, a solid form such as a crystalline, film, or precipitate of the same or similar composition is expected to dissolve more slowly.

'832 patent, col. 1, lines 24-28, 41-43, 47-50, col. 4, lines 4-31 (emphasis added). The "lasting contact" of the invention of the '832 patent is here sharply contrasted with the "very limited residence time" and "limited or poor adhesion" obtained with a gel.

This is a very strong teaching away from the use of gels. The '832 patent itself compares gels with the invention and finds them undesirable, inter alia, because of their "short residence time" and "limited or poor adhesion." "It is improper to combine references where the references teach away from their combination." MPEP § 2145.X.D.2. Here, the combination

claimed by applicants comprises a hydrogel (which will generally be a gel when in a moist environment), while the '832 teaches away from the use of gels. The combination is thus improper.

Second, the Examiner acknowledges that the limitation "a complementary oligomer capable of hydrogen or electrostatic bonding to the hydrophilic polymer" of claim 1 is not met in the '832 reference. (Action at 5.) No surprise here: a complementary oligomer as claimed would tend to[1] produce a hydrogel (at least with PVP), and that is one thing that the '832 patent definitely does not want. Given this deficiency in the '832, the Examiner looks to the laundry list of plasticizers in the '751, which has some overlap with the list of possible complementary oligomers in the present application. The Examiner states that plasticizers "have the advantage of providing soft flexible film," so one of skill in the art would wish to add one to the '832 for that reason. (Action at 6.)

This reasoning is not well taken. Plasticizers that can actually serve as complementary oligomers in the sense of claim 1, establishing the hydrogen or electrostatic bonds recited in the claim, will tend to produce a gel, which the '832 patent teaches away from. There is also no indication that the '832 patent actually wants or desires a soft flexible film. Rather the '832 patent seems to be content with the softness and flexibility which is achieved when the disclosed device is put in place: "Water absorption softens the device quickly, diminishing and eliminating the foreign body sensation." '832 col. 5, lines 16-18. There is no other reference to softness in the '832 patent's description of its invention. The Examiner's stated reason to combine the '832 with the '751 is therefore not legally appropriate.[2]

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1. Whether a hydrogel would actually result would depend on the exact proportions of the complementary oligomer and any hydrophilic polymer with which it can form hydrogen or electrostatic bonds.
2. The Examiner also reasons, citing '751 col. 4, lines 28-37, that a plasticizer would "eliminat[e] the disadvantage of physical properties at the administration site by enhancing the release properties of the active agent." (Action at 6.) This reasoning is also not well taken. (A) The cited passage refers not to what can be achieved by having a plasticizer versus not having one, but rather refers to "changing the kinds of the plasticizers to be used or . . . employing two or more of these in combination." (B) The "disadvantage of physical properties" appears to refer to softness, which is not something that the primary reference '832 wants, as explained above. The effect of plasticizers on "release properties" of the active agent is not described elsewhere in the '751, so that one would not even know from the '751 what direction of change in what "release property" would be achieved, or with what plasticizer or combination of plasticizers. (C) Furthermore, the active in the '751 is a prostaglandin and thus any information the '751 gives about plasticizers' effect on "release properties" would on first blush only be taken as

Third, claim 1 requires that the backing layer dissolve more slowly than the hydrogel. The '832 teaches the ***exact opposite***: "the adhesive layer, which is closest to the treatment site . . . will have a slower dissolution time, given that the backing layer protects the interior, adhesive layer and *will dissolve first*." '832 col. 5, lines 33-36. The '751 patent, as explained above, cannot cure this deficiency in the '832, since the '751's "backing layer" (there called a "drug delivery layer") also dissolves faster, not slower. Thus, the combination of the '832 with the '751, even if legally permissible, *does not produce what is claimed here*, namely a backing layer "that erodes in a moist environment at a slower rate than the hydrogel."

Obviousness combination adding the '453 patent. Because the '832 teaches away from the hydrogel limitation in the only independent claims 1 and 50, it certainly cannot be used to reject any claim, even if a third patent is added – the '453. The Examiner's sole reasoning for making the three-patent combination is "the combined teachings of US '832 and. US '751 desired to deliver active agent to the mucus membranes and also provided enhanced delivery." This is a wholly generic justification applicable to mucosal delivery of any active with any system described in a patent. This is not the specific justification of why a combination would be made, which is legally required to make out a prima facie case of obviousness. See MPEP §2142. In addition, the fact that the '832 and '751 together do not in fact give what is claimed as explained above further shows that the claim rejection based on obviousness over the '832, '751, and '453 is not well taken.

Conclusion. It is hoped that the present response adequately explains why the Examiner's rejections are not well founded. If the Examiner has any questions about this

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applicable to prostaglandins, a rather unusual drug class. For all of these reasons, the citation to '751 col. 4, lines 28-37, is also not a proper motivation to combine the '832 with the '751.

response, it is respectfully requested that she telephone the undersigned attorney at his direct dial (650) 251-7712.

Respectfully submitted.

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